

CLAIMS

What is claimed is:

1. A method for isolating one or more T cells that cross-react with a self-antigen and a foreign antigen, comprising:
 - (a) incubating a sample comprising T cells with an antigen that comprises an epitope present in the self-antigen and the foreign antigen, and optionally one or more autoantigens, wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.
2. The method of claim 1, wherein the self-antigen comprises a sequence of residues 96-102 of myelin basic protein, residues 93-105 of myelin basic protein, or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen comprises a sequence of residues 4-10 of human herpesvirus-6 U24, residues 1-13 of human herpesvirus-6 U24, or a fragment, variant, analog, homolog or derivative thereof.
3. The method of claims 1 or 2, wherein the autoantigen is selected from the group consisting of myelin basic protein, proteolipid protein, myelin oligodendrocyte glycoprotein, collagen type II peptides, heat shock protein, MAGE, PSA, CA125, GAD protein, and tumor associated antigen.
4. The method of claims 1 or 2, wherein the autoantigen comprises an immunodominant epitope of a member selected from the group consisting of myelin basic protein, proteolipid protein, myelin oligodendrocyte glycoprotein, collagen type II peptides, heat shock protein, MAGE, PSA, CA125, GAD protein, and tumor associated antigen.
5. The method of claim 4, wherein said immunodominant epitope is selected from the group consisting of residues 83-99 of myelin basic protein and residues 151-170 of myelin basic protein.
6. A method for isolating one or more T cells that cross-react with an self-antigen and a foreign antigen, comprising:

- (a) incubating a sample comprising T cells with an antigen that comprises an epitope present in the self-antigen and the foreign antigen, and optionally one or more autoantigens; and
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13.

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.

7. The method of claim 6, wherein the self-antigen comprises a sequence of residues 96-102 of myelin basic protein, residues 93-105 of myelin basic protein, or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen comprises a sequence of residues 4-10 of human herpesvirus-6 U24, residues 1-13 of human herpesvirus-6 U24, or a fragment, variant, analog, homolog or derivative thereof.

8. The method of claims 6 or 7, wherein the autoantigen is selected from the group consisting of myelin basic protein, proteolipid protein, myelin oligodendrocyte glycoprotein, collagen type II peptides, heat shock protein, MAGE, PSA, CA125, GAD protein, and tumor associated antigen.

9. The method of claims 6 or 7, wherein the autoantigen comprises an immunodominant epitope of a member selected from the group consisting of myelin basic protein, proteolipid protein, myelin oligodendrocyte glycoprotein, collagen type II peptides, heat shock protein, MAGE, PSA, CA125, GAD protein, and tumor associated antigen.

10. The method of claim 9, wherein said immunodominant epitope is selected from the group consisting of residues 83-99 of myelin basic protein and residues 151-170 of myelin basic protein.

11. The method of claim 7, wherein the cells expressing said first and said second markers are selected using antibodies to said first and second markers respectively, or optionally a bi-specific antibody which binds both first and second markers in combination with an antibody which binds said second marker.

12. The method of claim 11, wherein one or more of said antibodies is fluorescently labeled.

13. The method of claim 12, wherein said T cell is selected by fluorescent activated cell sorting.

14. The method of claim 11, wherein said first antibody is conjugated to a magnetic microbead.

15. The method of claim 14, wherein said T cell is selected by magnetic activated cell sorting

16. A composition comprising one or more T cells that cross-react with a self-antigen and a foreign antigen,

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof,

wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof, and

wherein the cross-reacting T cells are enriched with respect to other T cells that react with the self-antigen.

17. The composition of claim 16, wherein the self-antigen comprises a sequence of residues 96-102 of myelin basic protein, residues 93-105 of myelin basic protein, or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen comprises a sequence of residues 4-10 of human herpesvirus-6 U24, residues 1-13 of human herpesvirus-6 U24, or a fragment, variant, analog, homolog or derivative thereof.

18. A method for quantifying the number of T cells in a sample that cross-react with an self-antigen and a foreign antigen comprising:

- (a) incubating a sample comprising T cells with an antigen that comprises an epitope present in the self-antigen and the foreign antigen, and optionally one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13; and

- (c) determining the number of T cells selected by step (b).

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.

19. A method for diagnosing an autoimmune disease in a patient, comprising:

- (a) incubating a sample derived from said patient comprising T cells with an antigen that comprises an epitope present in a self-antigen and a foreign antigen, and optionally one or more autoantigens; and
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13.

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.

20. A method for monitoring an autoimmune disease in a patient, comprising:

- (a) incubating a sample derived from said patient comprising T cells with an antigen that comprises an epitope present in a self-antigen and a foreign antigen, and optionally one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13; and
- (c) determining the number of T cells selected by step (b),

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.

21. A method for treating an autoimmune disease in a patient, comprising:
- (a) incubating a sample derived from said patient comprising T cells with an antigen that comprises an epitope present in a self-antigen and a foreign antigen, and optionally one or more autoantigens;
 - (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13;
 - (c) inactivating the T cells selected by step (b); and
 - (d) administering the T cells inactivated by step (c) to said patient,

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.

22. A method for producing a composition for the treatment of an autoimmune disease in a patient, comprising:

- (a) incubating a sample derived from said patient comprising T cells with an antigen that comprises an epitope present in a self-antigen and a foreign antigen, and optionally one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13; and
- (c) inactivating the T cells selected by step (b),

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.

23. The method of claims 21 or 22 further comprising expanding the number of T cells selected in step (b).

24. A composition for the treatment of a patient with an autoimmune disease produced by the method of claim 21 or 22.

25. A method for isolating a nucleic acid encoding a T cell receptor, or a portion thereof, wherein said T cell receptor is specific for a self-antigen and a foreign antigen, comprising:

- (a) incubating a sample comprising T cells with an antigen that comprises an epitope present in the self-antigen and the foreign antigen;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13; and
- (c) amplifying the nucleic acid encoding said T cell receptor from a T cell isolated by step (b) using at least one first primer specific for the variable region of the T cell receptor gene and a second primer specific for the constant region of the T cell receptor gene,

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.

26. A method for isolating one or more nucleic acids encoding one or more T cell receptors, or a portion thereof, wherein said one or more T cell receptors are specific for a self-antigen and a foreign antigen, comprising:

- (a) incubating a sample comprising T cells with an antigen that comprises an epitope present in the self-antigen and the foreign antigen, and optionally one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13; and
- (c) amplifying said one or more nucleic acids encoding said T cell receptors from T cells isolated by step (b) using at least one first primer specific for the variable region of the T cell receptor gene

and a second primer specific for the constant region of the T cell receptor gene.

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.

27. A method for determining the repertoire of nucleic acids encoding one or more T cell receptors, or a portion thereof, in a patient, wherein said one or more T cell receptors are specific for a self-antigen and a foreign antigen:

- (a) incubating a sample derived from said patient comprising T cells with an antigen that comprises an epitope present in a self-antigen and a foreign antigen, and optionally one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2, IFN γ , TNF α , IL5, IL-10 and IL-13;
- (c) amplifying said one or more nucleic acids encoding said T cell receptors from T cells isolated by step (b) using at least one first primer specific for the variable region of the T cell receptor gene and a second primer specific for the constant region of the T cell receptor gene; and
- (d) determining the nucleotide sequence of the one or more nucleic acids amplified by step (c),

wherein the self-antigen is myelin basic protein or a fragment, variant, analog, homolog or derivative thereof, and wherein the foreign antigen is human herpesvirus-6 U24 or a fragment, variant, analog, homolog or derivative thereof.